

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
20 January 2005 (20.01.2005)

PCT

(10) International Publication Number
WO 2005/005475 A3

(51) International Patent Classification⁷: A61P 35/00, A61K 45/00

(21) International Application Number: PCT/EP2004/007527

(22) International Filing Date: 8 July 2004 (08.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data: 03015788.7 10 July 2003 (10.07.2003) EP

(71) Applicant (for all designated States except US): MAX-PLANCK-GESELLSCHAFT ZUR FÖRDERUNG DER WISSENSCHAFTEN E.V. [DE/DE]; Hofgartenstr. 8, 80539 München (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ZERIAL, Marino [IT/DE]; Loschwitzer Strasse 35, 01309 Dresden (DE). MIACZYNsKA, Marta [PL/DE]; Hübnerplatz 4, 01309 Dresden (DE).

(74) Agent: DEHMEL, Albrecht; Dehmel & Bettenhausen, Patent- und Rechtsanwälte, Herzogspitalstrasse 11, 80331 München (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
26 May 2005

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: APPL PROTEINS AS RAB5 EFFECTORS

(57) Abstract: The present invention relates to an in vivo-assay to screen for anti-proliferative drugs, the assay comprising the steps of: (a) contacting cells of a primary cell culture or of an established cell line with a candidate substance, (b) subsequently or concomitantly with a candidate substance, contacting the cells with a growth factor, (c) processing the cells for immunofluorescence staining to detect APPL1 and APPL2 using an anti-APPL1 and/or 2 antibody, or alternatively using GFP-tagged APPL proteins stably or transiently expressed by the cells via transfection, (d) assessing the degree of colocalisation of APPL1 and/or 2 and the growth factor, the solubilisation of APPL1 and/or 2 and their translocation to the nucleus, (e) repeating steps (b) to (d) with cells not previously treated with the candidate substance, and (f) comparing the degree of colocalisation of APPL1 and/or 2 and the growth factor, the solubilisation of APPL1 and/or 2 and their translocation to the nucleus between the cells not previously treated with the candidate substance (untreated cells) and cells treated with the candidate substance (treated cells), wherein an altered degree of colocalisation of APPL1 and/or 2 and the growth factor, an altered solubilisation of APPL1 and/or 2 and/or their altered translocation to the nucleus in the treated vs. the untreated cells identifies the candidate substance as an anti-proliferative drug.

WO 2005/005475 A3